REMARKS

Applicants thank the Examiner for removing the rejection of the claims under 35 U.S.C. §101. Claims 24-35 and 56-75 are pending. Applicants respectfully request reconsideration of the rejections in view of the following remarks.

I. Information Disclosure Statement

On page 2 of Paper No. 26, the Examiner states, "In Paper No.25, Applicant refers to several articles that are allegedly cited on an IDS. However, no IDS was filed with the Paper and the references referred to do not appear on the only IDS presently in the case (filed 15 February 2002)."

Applicants respectfully disagree and submit that two separate Information Disclosure Statements and accompanying Form PTO/SB/08's have been submitted by Applicants in this case. The first IDS was submitted on August 4, 2003 with references A-O, as indicated by the date-stamped Return Receipt postcard submitted herewith. The second IDS was submitted on December 1, 2003 with references P-Y, as indicated by the date-stamped Return Receipt postcard also submitted herewith. A copy of both Information Disclosure Statements and PTO/SB/08 forms are also submitted herewith. Applicants have not yet received signed copies of the PTO/SB/08 forms that indicate the Examiner has considered all references. Applicants will gladly re-submit references A-Y if necessary, upon request by the Examiner.

II. Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph

Claims 24-35 and 56-75 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement in the specification. *See* page 3 of Paper No. 26. Specifically, the Examiner agrees that the use of the instant invention for the diagnosis of pre-eclampsia is a specific and substantial utility, but contends, "at the time of filing, the skilled artisan would not know how to use the clamed invention, or a diagnostic or therapeutic agent developed therewith, to diagnose or treat preeclampsia without specific guidance as to how the instant neurokinin B was involved in placental blood flow in the pathological state." The Examiner further asserts that Severini *et al.* (2002) 54:285-322 teaches that the effect of tachykinins is irregular and unpredictable, in most cases inducing vasodilation and hypotension while in some cases inducing vasoconstriction and hypertension. Thus, the Examiner concludes "based on these teachings, the skilled artisan

would not know how to use a newly discovered tachykinin expressed in the placenta, or diagnostic or therapeutic agents developed therewith, to diagnose or treat preeclampsia because one of ordinary skill would not be able to predict whether the tachykinin is expressed in such a way as to contribute to the preeclampsia phenotype or has vasoconstrictor or vasodilator activity." *See* lines 8-13 on page 5 of Paper No. 26.

In response, Applicants respectfully disagree and traverse this rejection.

Preliminarily, Applicants appreciate that the current Office Action was made non-final in order for Applicants to respond to the present rejection. Applicants respectfully point out that according to M.P.E.P. § 2164.01(b), "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied." *Citing In re Fisher*, 427 F2d 833,839; 166 USPZ 18, 24 (CCPA 1970). In order to enable the claimed invention as required by 35 U.S.C. § 112, the specification need only enable a person of ordinary skill in the art to make the claimed polypeptides and practice at least a single use, and this use can be confirmed, without undue experimentation, by following procedures either described in the specification or otherwise known in the art. As far as determining whether experimentation is undue, the factors that can be considered have been listed in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. Furthermore, a patent applicant's specification disclosure, which contains a teaching of how to make and use the invention, must be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *In re Marzocchi*, 439 F.2d 220, 223-224, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971).

Applicants note that of the Wands factors cited by the Examiner on pages 3-6 in Paper No. 26, the Examiner is particularly concerned with (a) the state of the art and level of predictability in the art; and (b) amount of direction provided as reasons for issuing the current 35 U.S.C. § 112, first paragraph rejection. Applicants respectfully submit that neither of these Wands factors are problematic for the following reasons.

Regarding the state of the art and level of predictability in the art, Applicants respectfully submit that, as disclosed at lines 1-4 on page 35 of the specification, the HPMBQ91 polypeptide of the instant invention shares sequence homology with bovine preprotachykinin B (Accession No. 163590), which was known in the art at the earliest

effective filing date of the instant application to be the precursor for bovine neurokinin B (also known as neuromedin K; *see* Kotani *et al.*, 1986 submitted as reference C on August 4, 2003). Furthermore, it was additionally known that neurokinin B is processed to an active decapeptide having the amino acid sequence DMHDFFVGLM (*see* Kotani *et al.* and the first two sentences of the abstract in Lang *et al.*, submitted as reference Y with the IDS submitted on December 1, 2003). This decapeptide is conserved in the HPMBQ91 polypeptide of the instant invention, as illustrated in the alignment submitted as Exhibit A with Applicants response dated August 4, 2003 (*see* amino acid residues 81-90 of HPMBQ91 sequence). Hence, it would have been readily apparent to one of skill in the art at the time of filing that the polypeptide of the instant invention is the human ortholog of preprotachykinin B/neurokinin B.

Applicants additionally submit that it was also known in the art at the earliest priority date of the instant invention that neurokinin B from other species elicits a hypertensive effect. For example, neurokinin B is hypertensive in conscious, freely moving animals as well as in some anaesthetized animals, as described in Nagashima *et al.* (1989, submitted herewith as reference Z) and in Roccon *et al.* (1996, submitted herewith as reference AA). Nagashima *et al.* disclose that injection of senktide, a neurokinin B receptor stimulant used to mimic the effect of neurokinin B, caused prolonged hypertension in anaesthetized rats, and that this response was dose-dependent. *See* Nagashima *et al.*, right column of page 395 and Figure 3C. Roccon *et al.* disclose that neurokinin B, [MePhe7]neurokinin B and senktide all produced dose-related increases in blood pressure in conscious, freely moving guinea-pigs (as well as in anaesthetized guinea-pigs; *see* Roccon *et al.*, last paragraph of right column on page 1097, Figure 2, and second paragraph of left column on page 1101). This indicates the hypertensive effect of neurokinin B in un-anaesthesized animals although neurokinin B can elicit a hypotensive effect in anaesthetized animals (see right column of page 1095 of Roccon et al.). Roccon *et al.* additionally reference the results of an earlier experiment in which senktide and Me-Phe7]neurokinin B did not modify blood pressure in conscious, freely moving Wistar Kyoto rats that were *already spontaneously hypertensive* (*see* reference to Pompei *et al.*, 1992, in right column on page 1095 of Roccon *et al.*). These results further illustrate that neurokinin B is likely hypertensive although this affect was possibly masked by the fact that the animals were already spontaneously hypertensive. Thus, Applicants submit that based on the known hypertensive effect of neurokinin B combined with the disclosed

expression of the human protein in the placenta, one of skill in the art at the time of filing would have expected an increase in the level of the HPMBQ91 polypeptide of the instant invention to be associated with preeclampsia and indicative of the disorder.

Applicants further submit that the present specification provides ample guidance for one of ordinary skill in the art to routinely use the claimed polypeptides. In particular, the specification teaches methods for using the claimed polypeptides of the invention "for the diagnosis and treatment of reproductive and embryonic disorders" (page 36, lines 11-12), such as preeclampsia or eclampsia (page 229, line 10). Methods of detecting abnormal levels of a polypeptide in a biological sample are disclosed at page 303, line 28 through page 304, line 23. Given the foregoing teachings of the specification, it cannot be said that the invention as claimed is not enabled. *See In re Wands*, 8 U.S.P.Q.2d at 1404; *Ex parte Mark*, 12 U.S.P.Q.2d 1904, 1906-1907 (B.P.A.I. 1989). Applicants submit that the skilled protein chemist or molecular biologist, enlightened by the teachings of the present specification, is more than capable of routinely using the claimed polypeptides for any of the uses discussed above.

Thus, based on the disclosure of the present specification and the knowledge of one of ordinary skill in the art at the time the application was filed, it is clear that one of ordinary skill in the art would have been able to use the invention commensurate with the scope of the claims. Accordingly, Applicants submit that the instant invention is fully enabled as required under 35 U.S.C. section 112, first paragraph. Thus, Applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application. Applicants believe that this application is in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the examination of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an additional extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Dated: February 23, 2004

Respectfully submitted,

By 

Janet Martineau
Registration No.: 46,903
HUMAN GENOME SCIENCES, INC.
9410 Key West Avenue
Rockville, Maryland 20850
(301) 315-2723

KKH/JMM/KM/lcc